Remarks

I. Status of the Application and Claims

As originally filed, the present application had a total of 12 claims. These were all previously cancelled and replaced with claims 13-22. New claims 23-26 have been added herein. Thus, upon entry of the present amendments, the claims pending in the application will be claims 13-26.

II. The Amendments

Claim 13 has been amended to incorporate the requirements of previous claims 15 and 17. In particular, paragraph aii) was amended to indicate that the protein referred to is encoded by the nucleotide sequence of SEQ ID NO:3 (see claim 15 prior to amendment) and paragraph aiv) was added to indicate that overexpression is achieved by increasing the copy number of DNA or by operably linking DNA to a promoter (see claim 17 prior to amendment).

The dependency of claim 15 was changed and claim 17 was narrowed. Claim 18 was amended to correct an obvious typographical error. Claim 22 was amended to eliminate language that the Examiner appears to have found confusing and now simply refers to genes that are "attenuated," a term that is clearly defined in the specification.

New claim 23 is generally similar to claim 13 but includes the requirement that bacteria transport glucose by a PEP-dependent phosphotransferase (PTS) pathway. This limitation was included to distinguish the claimed method from methods reported in references cited by the Examiner in rejecting claims under 35 USC §102. The cited references describe methods that utilize bacteria which have undergone mutations that block their PTS pathway. These bacteria are excluded from claim 23. Although the exact phrase used in the claim is not present in the specification, all of the bacteria siggested for use on page 8 of the specification as well as the bacteria used in Example 2 have intact PTS pathways that transport glucose, *i.e.*, they grow readily using glucose as an energy source. Thus, the limitation is inherently present in the specification. In this regard, it should also be noted that genes involved in the PTS pathway are among those listed in claim 21 as being optionally overexpressed in the bacteria.

The amendments do not add new matter to the application and their entry is therefore respectfully requested.

III. Claim Objections

On pages 2 and 3 of the Office Action, the Examiner objects to claim 13 because a comma is missing between the words "starch" and "cellulose." This has now been added.

In addition, the Examiner objects to claim 13 because the conjunction "and" is needed between step a and step b. Applicant has amended claim 13 so that the word "and" now comes at the end of paragraph aiv) and immediately before step b).

The Rejections

I. Rejection of Claims Under 35 U.S.C. § 112, Second Paragraph

On pages 3 and 4 of the Office Action, the Examiner makes several rejections under 35 USC § 112, second paragraph. These are presented in items 7-10. Applicant responds to each allegation below.

A. Response to Items 7 and 8

In items 7 and 8, claims 13-22 are rejected based upon the allegation that the phrase "overexpressed" or "overexpresses" is indefinite.

Applicant respectfully traverses this rejection.

It is respectfully submitted that the meaning of the terms objected to by the Examiner is provided in the specification on page 7, lines 1-12. This reads as follows:

> The word "overexpression," in this connection, describes the increase in intracellular activity or concentration of one or more enzymes or proteins, in a microorganism, which are coded for by the corresponding DNA. Overexpression may be accomplished, for example, by increasing the copy number of the gene or genes by at least one (1) copy, by using a strong promoter, or by combining these measures.
>
> As a result of overexpression, the activity or concentration of the corresponding protein may be increased by at least 10%, 25%, 50%, 75%, 100%, 150%, 200%, 300%, 400% or 500%, at most up to 1000% or 2000%, with respect to the wild type protein or the activity or concentration of the protein in the starting microorganism. The starting microorganism or parent

> strain is understood to be the microorganism on which the measures to achieve overexpression are performed.

It should be clear from the paragraphs quoted above that overexpression refers to an increase in activity measured relative to either the starting microorganism or parent strain. Thus, for example, overexpression of a protein or gene may be achieved by recombinantly transfecting a microorganism with a gene encoding the protein and its increase would be measured relative to the microorganism prior to transfection.

B. Response to Item 9

In item 9, the Examiner rejects claims 21 and 22 based upon the allegation that it is unclear whether these claims refer to all forms of the recited genes or to the species that are recited in the specification.

In response, Applicant submits that the terms in patent claims are interpreted based upon their use in the specification. In the present case, the specification provides a specific reference for each gene that is recited and there is never a suggestion that the invention includes anything broader than these specific genes. Thus, Applicant submits that it should be clear that the claims do not refer to all forms of the genes but to the specific forms that are presented in the specification. The only other genes encompassed by the claims are those that, under the doctrine of equivalents, would be considered substantially the same as the species defined in the specification.

C. Response to Item 10

In item 10, the Examiner rejects claim 22 based upon the allegation that it is unclear what is meant by saying that gene expression is reduced.

In response, Applicant has amended claim 22 so that it now refers to genes that are "attenuated," a term whose meaning should be clear from the definition on page 16 (line 20-27). This reads as follows:

> The expression "attenuation" in this connection describes the reduction in or switching off of intracellular activity or concentration of one or more enzymes or proteins in a microorganism by, for example: using a weak promoter; using a gene or allele which codes for a corresponding enzyme or protein with a lower activity; or by inactivating the corresponding enzyme or protein or gene;

> and optionally by combining these measures. Due to attenuation, the activity or concentration of the corresponding protein is generally lowered to 0 to 75%, 0 to 50%, 0 to 25%, 0 to 10% or 0 to 5% of the activity or concentration of the wild-type protein in the starting microorganism.

In light of the above definition, Applicant submits that it should be clear that an attenuated gene is one whose activity or concentration has been reduced relative to the activity or concentration in the wild type or starting microorganism.

II. Rejection of Claims Under 35 U.S.C. § 112, First Paragraph

On pages 4-8 of the Office Action, the Examiner makes two rejections under the first paragraph of 35 USC § 112. These are set forth in items 11 and12. Applicant responds to each rejection below.

A. Response to Item 11

In item 11, claims 13-16 and 18-22 are rejected as failing to meet the written description requirement of patentability.

In response, Applicant has incorporated the limitations of claim 17 into claim 13. Since claim 17 was not included as part of the rejection, Applicant respectfully submits that this amendment should be sufficient to obviate the rejection.

B. Response to Item 12

In item 12, on page 6 of the Office Action, the Examiner rejects claim 13-16 and 18-22 as failing to meet the enablement requirement of 35 USC § 112. As with the rejection in item 11, claim 17 is not included. Thus, by including the limitations of claim 17 in claim 13, Applicant submits that the present rejection has been overcome.

III. Rejection of Claims Under 35 U.S.C. § 102

On pages 9-12 of the Office Action, the Examiner makes two separate rejections under 35 USC § 102. In item 13, claims 13-14 and 17-20 are rejected as anticipated by Valle (US 2002/0155521) as evidenced by Blattner *et al.* (*Science 277*:1453-1474 (1997)). In item 14, these same claims are rejected under 35 USC § 102(a) as being anticipated by Hernandez-

Montalvo *et al.* (*Biotechnol. Bioeng. 83*:687-694 (2003)) as evidenced by Blattner *et al.* and Lee *et al.* (*J. Bacteriol. 185*:5442-5451 (1997)).

In response, Applicant has amended claim 13 to include the limitations of claim 15. Since this claim was not included in either of the rejections made under section 102, Applicant respectfully submits that the Examiner's rejection has been overcome both with respect to this claim and for dependent claims 14-22.

New claim 23 includes the requirement that the bacteria used in the claimed process transport glucose by a PEP-dependent phosphotransferase (PTS) pathway. Since both the Valle reference and the Hernandez-Montalvo reference only examined the effect of galP in PTS^- cells and fail to suggest that increasing expression of galP in PTS^+ cells may increase amino acid production, this limitation should be sufficient to overcome the rejection of claims under 35 USC §102.

The Valle reference was fully discussed in Applicants response filed on September 15, 2006, As indicated therein, Valle actually expressly indicates that galP-based transport is of no physiological relevance unless the PTS pathway is blocked (see paragraph [0034] on page 4 of the reference).

Hernández-Montalvo describes experiments in which the E. coli PTS^-/glu^- strain VH32 is transformed with plasmids containing galP and glk genes driven by a trc promoter (Table II, p. 691). As a result of this transformation, the strain acquires the $glucose^+$ phenotype (page 691, right column, line 1-12). It should be noted however that transforming strain VH32 with a galP gene does not increase the copy number of an existing active galP gene in the microorganisms. Instead, the gene is highly expressed because the plasmid comprises an active promoter (trcI, page 691, left column). Thus there is a second basis for concluding that claim 23 (and dependent claims 24-26) are not anticipated by this reference.

Since it should be readily apparent that the deficiencies in Valle and Hernández-Montalvo cannot be cured by either Blattner *et al.* or Lee *et al.*, it is respectfully requested that the rejection under 35 USC §102 be withdrawn.

IV. Rejection of Claims Under 35 U.S.C. §§ 103

On pages 13-14 of the Office Action, claims 21 and 22 are rejected under 35 USC §103. In item 15, claim 21 is rejected based upon Valle in combination with Debabov *et al.* (US 6,132,999). In item 16, claim 22 is rejected based upon Valle in combination with a second Debabov reference (US 5,705,371).

Neither of the rejections that are made under section 103, include either claim 15 or 17. Since the limitations of both of these claims have been incorporated into claims 13, and by extension, are also part of dependent claims 21and 22, Applicant respectfully submits that the Examiner's rejection has been obviated.

Conclusion

In light of the amendments and discussion above, Applicant believes that all of the Examiner's rejections have been overcome. It is therefore respectfully requested that these rejections be withdrawn and that the claims now pending be allowed. Early notice to this effect is earnestly solicited.

If, in the opinion of the Examiner, a phone call would help to expedite the prosecution of this application, the Examiner is invited to call Applicant's undersigned attorney at (240) 683-6165.

Respectfully submitted,

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